

Claims

1. A method of transdifferentiating mammalian non-pancreatic stem cells to enter the pancreatic differentiation pathway, comprising:

5 culturing said stem cells under conditions that permit the expression of pancreatic differentiation markers,

wherein said conditions are selected from the group consisting of:

a) culture conditions that promote cell clustering;

10 b) medium comprising an added factor that comprises at least one of glucagon-like peptide-1 (GLP-1), hepatocyte growth factor (HGF) and nicotinamide; and

c) conditions of both (a) and (b).

2. The method of claim 1 wherein the pancreatic markers that are expressed are selected from the group consisting of *Pdx-1*, *Isl-1*, *Pax-4*, *Pax-6*, *Glut-2*, *glucagon*,
15 *somatostatin*, *pancreatic peptide* (PP) and *insulin*.

3. The method of claim 1 wherein said transdifferentiated cells respond to contact with glucose by secretion of insulin.

20 4. The method of claim 1 wherein said culture conditions that promote cell clustering are low binding tissue culture plates, extracellular matrix, or both.

5. The method of claim 1 wherein said medium comprises one or more components selected from the group consisting of Dulbecco's Minimal Essential Medium (DMEM) with high glucose and sodium pyruvate; bovine serum albumin (BSA); 2-
25 mercaptoethanol; fetal calf serum (FCS); penicillin and streptomycin (Pen-Strep); insulin, transferrin and selenium (ITS); and Fungizone®.

30 6. The method of claim 1 wherein the added factors comprise GLP-1, HGF and nicotinamide.

7. The method of claim 6 wherein GLP-1 has a concentration of about 100 nM, HGF has a concentration of about 20 ng/ml and nicotinamide has a concentration of about 10 nM.

8. The method of claim 1 wherein said non-pancreatic stem cell is a mesenchymal stem cell (MSC).

5 9. The method of claim 8 wherein the MSC is CD105+, CD166+, CD29+ and CD44+.

10. The method of claim 1 wherein the stem cells are human.

10 11. A method of producing an endocrine hormone comprising the method of claim 1, and further comprising the step of continuing to culture said transdifferentiated cells in said medium, whereby an endocrine hormone may be produced.

12. A method of treating a mammal with a pancreatic disorder, comprising:

15 a) culturing non-pancreatic stem cells according to claim 1, whereby said stem cells transdifferentiate to the pancreatic differentiation pathway;

b) using a product of the culture of step (a) to treat said mammal.

20 13. The method of claim 12 wherein the pancreatic disorder is an insulin-requiring disorder.

14. The method of claim 12 wherein the product in step (b) is an endocrine hormone that is administered to the mammal.

25 15. The method of claim 12 wherein the product in step (b) is transdifferentiated cells, and said method further comprises:

c) implanting said product into said mammal.

30 16. The method of claim 15 wherein said implantation is in pancreatic, kidney or liver tissue, or in a subcutaneous pocket.

17. The method of claim 12 wherein said transdifferentiated stem cells are transdifferentiated MSCs.

18. The method of claim 12 wherein the non-pancreatic stem cells originate from an individual that is the same as the treated mammal of step (b).

19. The method of claim 15 wherein said implanted transdifferentiated cells are encapsulated in an endocrine hormone permeable capsule.

20. The method of claim 19 wherein said implanted, encapsulated, transdifferentiated cells are autologous to the mammal.

21. The method of claim 19 wherein said implanted, encapsulated, transdifferentiated cells are allogeneic to the mammal.

22. The transdifferentiated MSC produced by the method of claim 8.

23. A transdifferentiated MSC that expresses mRNA for *Isl-1*, *Pax-6*, *PP*, *insulin*, *glucagon* and *somatostatin*.

24. A transdifferentiated cell produced by the method of claim 1.

25. A therapeutic composition comprising a transdifferentiated MSC encapsulated in an endocrine hormone permeable capsule.